

## USE OF OLIGOSACCHARIDE FOR PREVENTING BLOOD CLOTTING IN EXTRACORPOREAL BLOOD CIRCUITS

This application is a divisional application of USSN 09/424,626 filed November 24, 1999, now pending.

The invention relates to the use of a certain oligosaccharide for the manufacture of a medicament for preventing blood clotting in extracorporeal blood circuits. Further the invention relates to a pharmaceutical composition for said use.

Blood clotting in extracorporeal blood circuits needs to be prevented. Otherwise, blood coagulation occurs as soon as blood contacts artificial surfaces. As a remedy, usually unfractionated heparin (UFH) or low molecular weight heparins (LMWH) are used as anticoagulants.

Both UFH and LMWH have an effect on several stages of the blood coagulation cascade, both inhibiting factor Xa and thrombin (factor IIa). Factor Xa catalyzes the generation of thrombin and subsequently thrombin regulates the last step in the coagulation cascade. The prime function of thrombin is the cleavage of fibrinogen to generate fibrin monomers, which form an insoluble gel by cross-linking, thereby initiating thrombus formation. UFH and LMWH have thrombolytic properties, i.e. they induce dissolution of the thrombus formed.

Contrary to UFH and LMWH, some synthetic oligosaccharides, especially oligosaccharides described in EP 84,999 and US 5,378,829, highly selectively inhibit factor Xa via antithrombin III (ATIII) but do not have any activity on thrombin. However, notwithstanding the absence of any capacity to inhibit thrombin or to promote thrombolysis, it appeared that those oligosaccharides inhibit thrombus formation, e.g. as occurring in extracorporeal blood circuits.

Thus, surprisingly, it has now been found that a synthetic oligosaccharide which is a selective inhibitor of factor Xa, acting via antithrombin III, is useful for preventing blood clotting in patients with an extracorporeal blood circuit.

The use of the oligosaccharide according to this invention results in effective and safe inhibition of blood clotting, e.g. in patients undergoing haemodialysis, without increased bleeding risks.

A preferred oligosaccharide for the use according to this invention is the pentasaccharide with the formula methyl O-(2-deoxy-2-sulphoamino-6-O-sulpho- $\alpha$ -D-glucopyranosyl)-(1 $\rightarrow$ 4)-O-( $\beta$ -D-glucopyranosyl uronic acid)-(1 $\rightarrow$ 4)-O-(2-deoxy-2-sulphoamino-3,6-di-O-sulpho- $\alpha$ -D-